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Investigating the relationship between the HJHS and HAL in routine clinical practice: A retrospective review.

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Abstract

Introduction: Comprehensive musculoskeletal assessment for monitoring joint health in haemophilia requires both physical assessment with Haemophilia Joint Health Score (HJHS) and assessment of self-reported function by Haemophilia Activities List (HAL).

Methods: Correlation between physical assessment and joint function was undertaken between HJHS and HAL in patients with SHA and SHB who had both assessments at the same visit over a one-year period.

Results: Data from 120 patients (96-SHA/ 24=SHB) with a median age 33 years (range 19-73) were included. Median total HJHS was 19, increasing with age; 18-30 yrs - 7, 31-50 yrs - 25 and 51-73 yrs- 44. Median total HAL score similarly was 80 with decreased function associated with increasing age; 18-30 yrs-90.4, 31-59 yrs - 71.7, 51-73 yrs -49.5. Median Total HJHS and HAL demonstrated strong correlation (r_s= 0.66, P<0.01). Moderate to strong correlation was seen across the entire age group between the HJHS LL and UL subtotals and corresponding limb HAL domains. Within age groups,

correlations were less significant particularly for the upper UL domains in HAL and the UL HJHS score.

Conclusion: HJHS and HAL showed moderate to strong correlation with discrepancy in some individual patients. Prospective studies are required to better understand the clinical utility of both especially in severe joint disease where HAL may have a pototential advantage.

Keywords: severe haemophilia, Haemophilia Joint Health Score, Haemophilia Activities List, Outcome measures, physical assessment, functional assessment

Word Count: 3238

Introduction

Modern haemophilia care within a comprehensive care setting ensures persons with severe haemophilia (PWSH) (A and B) are reviewed regularly to ascertain treatment effectiveness and for monitoring treatment and disease complications.[1] Although regular prophylaxis is the standard of care, recurrent bleeding into joints and muscles continues to be seen resulting in sequelae in the musculoskeletal (MSK) system with long term morbidity. Further, in developed countries, patients currently over the age of 65 had no access to prophylaxis until adulthood, and those over 45 years had no access to regular prophylaxis for most of their childhood and the majority of PWSH across the world continue to have limited access to regular prophylaxis.[2] Consequently most of these men have established multi joint arthropathy, usually affecting 4-6 of the main joints affected by haemophilia – the elbows, knees, ankles [3] and joint disease remains the main cause of morbidity in older persons with haemophilia.[4]

Traditionally in haemophilia care, factor VIII and IX trough levels and annualised bleed rates have been used to monitor the effectiveness of replacement therapy and regular prophylaxis.[5] There is increasing interest in using assessments that evaluate other aspects of a disease process that are personalised, and both patient reported and clinician led.[6, 7] Outcome assessments that evaluate both structure and function of the MSK system have been suggested to enhance the care of haemophilia patients.[8] The chosen assessments need to be sensitive to change in the outcomes of interest

for monitoring treatment efficacy and tailoring intervention strategies[9]. Further, it is preferable that such measures utilise a framework such as the World Health Organisation International Classification of Functioning, disability and health (ICF), that evaluates disease in the domains of body functions and structure, activity, participation and environmental context.[10]

A physical assessment typically includes an objective assessment of joint health and this can be standardised for monitoring over time and comparisons across centres. Such tools include World Federation of Haemophilia (WFH) physical examination score (aka Gilbert score) and Haemophilia Joint Health Score (HJHS).[9, 11] Assessments that have been developed for measuring activity and functional limitation for persons with haemophilia (PWH) include the Functional Independence Score in Haemophilia (FISH) and Haemophilia Activities List (HAL).[9, 12, 13] This dual approach is recommended by the World Federation of Haemophilia (WFH) in assessing health and disability in PWH.

The HJHS (vers 2.1), is a 9-item assessment tool developed and validated by the International Prophylaxis Study Group (IPSG) to identify early signs of joint damage in PWH. [14, 15] Its development was based on additions to the Gilbert scale and further merging of the Colorado and Stockholm scales.[16] It has been demonstrated to be reliable and sensitive in previous studies [16], although its specificity has not yet been determined. The Gilbert score is increasingly not considered to be sensitive for mild/moderate damage, resulting in an increasing uptake of the HJHS for surveillance

both in routine clinical practice and clinical trials, although the tool has not been validated in adults over the age of 30 nor for severe joint damage. [2]

The HAL is a haemophilia specific questionnaire evaluating self-perceived functional abilities covering daily function of the arms, legs and whole body, and is relatively quick and easy for the patient to complete. In adult PWH it has been shown to have reasonable reliability in measurement of function, although its sensitivity to measuring change over time has yet to be established.[12, 17]

Table 1. HJHS and HAL domain description

Although the WFH recommends the above tools [9] there is considerable uncertainty on the application of these tools for assessment of joint damage given the disparity in joint health associated with haemarthropathy in the haemophilia population, or if they offer day to day clinical utility. A recent review of practice with physiotherapists across the UK highlighted that the vast majority (83%) of those questioned used the HJHS in practice (in both paediatric and adult care), but only about 25% use the HAL or PedHAL. [18]

As there is limited published evidence on the value of these tools in routine clinical practice, the aim of this retrospective review was to evaluate in the first instance the relationship between joint health assessed physically and perceived function in our patient group. The primary objective was to describe the correlation between the

HJHS and the HAL across a range of age groups and joint damage in adult patients; and the secondary objective was to assess the correlation at the level of limbs and explore the potential for using HAL instead of HJHS in patients with widespread joint damage.

Methods

A retrospective review of PWSH A and B attending for review clinics for the period 1st April 2012-31st March 2013 was undertaken. Adult patients were eligible provided an assessment that included both the HJHS and the HAL had been completed at the same visit. Those with previous orthopaedic surgery were included in the dataset. As this was a review of existing practice and considered a service development by the NHS England research ethics committee, informed consent was not required.

Joint health was measured by the HJHS (vers 2.1), undertaken by an experienced haemophilia physiotherapist (PML) with extensive experience in the use of the assessment tool and relevant training. The HAL questionnaire was provided to the patient to complete on arrival at the clinic. On completion, the raw data for the HAL was transferred to an excel spreadsheet designed to calculate the values required for its clinical interpretation and use.

A structured form was used to extract information pertaining to the baseline diagnosis and major concomitant illnesses including HIV and hepatitis C infection. The HJHS subtotals for each individual joint assessed, a combined lower limb (LL) total of both ankles and knees, combined upper limb subtotal (both elbows) and the overall total

(including the gait score) were calculated. The individual domain values for the HAL components as well as the overall total, were included for each patient.

Statistics

Patient characteristics were described using descriptive statistics and Spearman's correlation analysis was completed using SPSS. Analysis included correlations between HJHS (total score, UL and LL subtotals) and HAL scores (total score and domain scores) by age group. Age was used as a surrogate marker for severity of joint damage. No corrections for multiple testing were carried out, since the primary interest was in the correlation between the total score of HALS and total joint score of all patients. Further correlations were calculated to back up this main analysis, to assess (a) if overall correlations held within specific age groups used as surrogate marker for joint damage (b) to assess whether correlations were specific to certain areas of the body.

Results

Patient characteristics

A total of 335 clinic attendances were available for review between 1st April 2012 and 31st March 2013. 120 PWSH A (n=96) and B (n=24) >18 years, who had both a HJHS and HAL completed at the same visit were eligible for inclusion in the final analysis, representing 74% of patients registered at this centre.

Patient characteristics are detailed in Table 2. The cohort median age was 33 years (range 19-73). Of the 120 patients, 77.5% (93/120) were receiving regular prophylaxis and 22.5% (27/120) were on-demand management. One had an inhibitor to factor VIII, and two an inhibitor to IX. Age was used as a surrogate for initiation and intensity of prophylaxis and three groups were defined. Most patients in age group of 18-30 years (n=50) have benefited from early onset prophylaxis and in the majority prophylaxis was initiated within the first few years of life. Patients in the 31-50 years (n=47) group would have been offered secondary prophylaxis in teens or as young adults and patients between 51-73 years (n=23) started in adulthood.

Table 2 – Patient Demographics

Table 3 - HJHS and HAL domain scores by age

Physical joint status (HJHS)

Summary scores of HJHS by age group are presented in Table 3. The median HJHS score for those aged 18-30 years was 7, increasing to 25 in those aged 31-50 yrs, and to 44 in those aged 51 yrs and over. The median scores progressively increased with increasing age reflecting increasing damage. Importantly the scores confirm previous findings that the ankles are the most commonly affected joint in all ages groups.[19] The range of movement (ROM) for patients who scored a maximum 3 (loss of >20°ROM) on the HJHS was also evaluated. In the elbow, loss of extension ranged from 21°to 90° and loss of flexion from 21°to 45°. In the knee, loss of extension ranged from 22° to 90°, and loss of flexion ranged from 42° to 90° and in the ankle loss of

plantarflexion ranged from 21° to 40°. Dorsiflexion is not included here as normative values for dorsiflexion mean that even with a zero-degree ROM measure may still score zero on the HJHS. The wide range of loss of ROM in joints categorised as markedly affected highlights the fact that the HJHS ~~has been developed for identifying early joint damage and its~~ sensitivity for monitoring progression of joint damage in severely affected patients is likely to be limited. [20]

Joint functional status (HAL)

Within all HAL domains relating to the lower limbs such as LSKS, LEGS, LOWBAS and LOWCOM the decrease in perceived function scores were substantially more marked in older individuals than those relating to the upper limb such as ARMS, SELFC, HOUSEH and UPPER. (Table 3). ~~The largest difference was 60 points in the LOWCOM domain between youngest and oldest groups, compared to a difference of only 28 in the self-care domain (even with the higher joint scores for elbow in this age group).~~

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Correlations

The correlation between the joint damage reported using HJHS and function as assessed by the patient was explored. Figure 1 demonstrates the overall relationship between HJHS and HAL in all patients below and above age 30. Spearman's Rho correlation was estimated to determine the relationship between the components of the HAL and the HJHS and presented in Table 4.

Table 4 – Correlation values between HAL domain scores and HJHS domain scores

Overall, there was a highly significant strong negative monotonic correlation between the total HJHS score and the total HAL score with increasing joint damage associated with poorer function (r=-0.66, p<0.001). Correlations were of comparable magnitude when examining the upper and lower limbs independently within HAL domains that were more limb specific (such as ARMS for UL), and although less strong in combined functional activities such as LEISPO, HOUSEH and SELFC, where the correlations remained moderately strong (p=<0.01)

Sub analysis within age groups showed some decrease in strength of correlation from the cohort total. In the 18-30 group, the self-care domain and UL score showed no significant correlation, whereas all other domains remained significant (p<0.01). The 31-50 age group had weaker correlations between the lower limb specific HAL domains of LEGS and LOWBAS, as well as overall functional domains of SELFC AND LSKS. Interestingly, even with greater joint damage in both the upper and lower limbs, the 51-73 year age group showed no significant correlation between total HJHS score and household, leisure or sports activity and between total LL HJHS scores and LEGS function.

Discussion:

Musculoskeletal assessment in a cohort of severe haemophilia A and B patients representative of patients across the UK with access to both primary and secondary prophylaxis, demonstrates increasingly severe joint damage with increasing age.

Increasing damage was associated with limitation of functional activities as reported by patients. Our data reveals a statistically significant, moderately strong correlation between total HJHS and total HAL across a wide age range and joint damage. Our data reiterates the observation that overall the ankle is the most affected joint, even in a younger age group with access to early prophylaxis. Importantly the strength of correlation did not increase with increasing joint damage and this might be related to the lack of sensitivity of either instrument to joint damage or patients' ability to compensate for functional limitations with life style adjustments.

The HJHS median scores in our cohort are comparable to the median scores in a study comparing outcomes of an intermediate and high dose prophylactic regime in younger adults. [21]. Our cohort with range of treatment had median HJHS of 7 and HAL score of 90.35 which are similar to the intermediate dose cohort (n=78) with a median HJHS of 9.0, and a HAL of 93. The high dose (n=50) reported a median HJHS of 4.0 and HAL of 99, highlighting the very positive effect of early haemophilia treatment.

The use of HJHS (version 1.0)and HAL in a younger cohort with limited joint damage has been explored in 22 patients (age range 14-30), with lower median HJHS score of 5.5 (range of 0-34), compared to 7 in our 18-30 cohort (range 0-63) with a weaker correlation of -0.40 between the HJHS and HAL total scores compared to a correlation of -0.65 in this cohort. [2]. In another international cross-sectional study of severe haemophilia patients on primary prophylaxis since median age of 3.4 years, no correlation was identified between total HAL and total HJHS when both objective and

subjective assessments of joint function were undertaken at a median 25.5 years (range 16.0-37.6).[22]

In a study exploring the risk factors for reduced physical activity and functional limitations in PWH, although haemophilic arthropathy was independently associated with reduced physical functioning and physical activity, much of the variability was not explained by arthropathy.[23] The authors suggested that other factors including motivation, expectation of activity and patient lifestyle might play a more a significant role in an individual's choice to participate, reiterating the need for dual assessment. This may help explain the poor correlation between joint disease and leg functions, self-care and household domains in the over 50's cohort analysed here.

In this cohort self-care, leisure and sport and household tasks demonstrated a good correlation with the elbow joint score when patients were analysed as single group. Suprisingly, no correlation was seen in the 18-30 group suggesting a lack of functional impairment with minimal joint damage, or a floor effect of the HAL. However, it also became less significant in the 51-73 age group, even in the presence of marked joint damage. In this group availability of treatment was markedly limited in their younger years resulting in elbow joint damage being established early. It is conceivable that the need to maintain independence in self-care ADLs resulted in an accommodation of the occupational limitation of the arthropathy. The lack of strong correlation may also be related to psychosocial adjustments (to their physical disability) that PWH undergo to cope with their reduced function and the proposed mechanisms used being that of

a task orientated one.[24, 25] Other possibilities include the lack of discrimination for severity of some aspects of joint damage in the current HJHS scoring system. The wide range of ROM in joints categorised as markedly affected (i.e. ROM loss score =3) highlights the potential ceiling effect of this domain score and its use in chronically damaged joints. This may be a weakness in using a tool designed for detection of early disease in older adults with well-established joint disease. Further, it does not include other joints that can be affected by haemarthropathy (such as the shoulder and hip) – both of which could affect overall perceived function. It may also highlight the possibility that the HAL is not asking the right questions in relation to function of the elbow, and more investigation is warranted of this.

Limitations of this analysis include the use of HJHS which has not been validated in adults with joint damage. HJHS was implemented as a pragmatic assessment tool for regular musculoskeletal reviews as it allowed the same assessment tool to be used for all age groups. Empirically we note that in those with already established joint damage, the joint score does not alter significantly from year to year. However, in a younger population it has been shown to be sensitive enough to discriminate between early and late prophylaxis, as well as inhibitor and non-inhibitor patients. [26]

As the HJHS is used for routine assessments, patients who had previous orthopaedic surgery were included in the dataset – as aspects of the HJHS and HAL can change for the better when a joint undergoes orthopaedic intervention (e.g. pain, ROM, swelling, crepitus), a potential limitation for evaluating the sensitivity and specificity of the

tools. Further, the HJHS total in some patients can be perceived as artificially low due to amputations, joint fusions, or limbs affected by polio for example. Whilst this may not capture the degree of actual joint disease secondary to haemophilic arthropathy, it may account for an improvement in physical health and perceived function. As a consequence, patients who had non evaluable (NE) joints as part of the assessment, even though older in age, had lower joint score totals. However, when using this score clinically, we are comparing the patient to themselves, and so it accommodates well to the individual presentation. This highlights the risk of using the HJHS in isolation and why care has to be taken when only looking at the HJHS total as an outcome measure.

~~Further, no other measures of quality of life or pain were included for correlation purposes.~~

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~~Our analysis shows a moderately strong correlation between HJHS and HAL with increasing joint damage reflecting how individuals view their function as a result. The HJHS currently does not categorise the joint damage by severity, and importantly, is skewed to identifying early damage. The wide ROM deficits seen in joints with maximal scores limits it utility as tool for identifying joints that might benefit from surgical or other interventions. In this context the HAL potentially may offer a better tool in PWH with widespread joint disease for monitoring joint function, with a focus on functional and participation issues rather than on joint health per se.~~

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Further research is needed to establish to establish the validity and specificity of current HJHS scoring system for assessing severity of joint disease, and the relative value of HJHS and HAL in identification of patients for surgical intervention, and their correlation to other health measures such as health related quality of life and pain.

In conclusion we have shown that comprehensive MSK assessment needs both a physical and functional assessment as neither can be used to categorise the severity of joint damage. Further, our data suggests that with widespread multi-joint involvement, the joint score alone is not useful in identifying potential issues. The use of the HJHS and HAL with those with mild to moderate joint disease would appear to offer clinical value, whilst the HAL independently may be more useful in those with widespread joint disease. As PWSH and multi-arthropathy continue to move into older age, we must ensure that services meet their needs. It is also imperative that assessments, both patient informed and clinician led, help ensure that subsequent interventions are evaluated by the most appropriate and useful outcome for the patient and healthcare professional.

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PML and PC contributed to the design of the study, RM and PC performed the statistical analysis, PML wrote the first draft of the paper, all authors contributed to the interpretation of the data and to critical revision of the manuscript.

Disclosures:

All authors state that they have no competing interests which might be perceived as posing a conflict or bias.

Table 1- HJHS and HAL domain descriptions

HJHS scoring domains (6 joints – Right/Left: elbow, knee, ankle)	HAL domains 42 multiple choice questions One month recall

Swelling (0-3) Duration of swelling (0-1) Muscle atrophy (0-2) Crepitus on motion (0-2) Flexion loss (0-3) Extension loss (0-3) Joint pain (0-2) Strength (0-4) Global gait score (0-4)	LSKS – Lying/ Sitting/ Kneeling/ Standing (8 items) LEGS- Function of the legs (9 items) ARMS- Function of the arms (4 items) TRANS - Use of transportation (3 items) SELFC - Self-care (5 items) HOUSEH - Household tasks (6 items) LEISPO - Leisure Activities and sports (7 items) <u>Combined component scoring from above domains:</u> UPPER – Combined upper limb domain specific LOWBAS – Basic lower limb function LOWCOM – Complex lower limb function
Score of 0-20 per joint Plus global gait score (observed) Total available score = 124	Score range = 0-100 (for both grand total and per domain) (0= very poor function, 100 = no functional issue)

Table 2 – Patient demographics

Patient numbers	N= 120 males
Diagnosis	SHA = 96, SHB= 24
Treatment regime	Prophylaxis = 93 On Demand = 27
Age range	19-73 (median 33)
Co-infection	HCV = 14, HIV= 14, HCV & HIV= 6
Inhibitor	FVIII= 1, FIX = 2
Orthopaedic surgery	Total hip replacement - 4 Total knee Replacement – 24 Total ankle replacement – 2 Radial head excision – 2 Ankle debridement – 2 Ankle arthrodesis - 6

Table 3 – HJHS and HAL domain scores by age

		Age		
	Total cohort (N=120)	**18-30** (N=50)	**31-50** (N=47)	**51-73** (N=23)
SHA/SHB (N=120)	98/22	39/11	40/7	17/6
		HJHS scores: Median (Range)		
Total HJHS	19 (IQR 7-39) (0-114)	7 (IQR 1-14) (0-63)	25 (IQR 15-41) (4-64)	44 (IQR 21-57) (14-114)
Total Elbows (R&L)	4 (0-13)	0 (0-3)	7 (0-13)	14 (9-23)
Total Knees (R&L)	2 (0-7)	0 (0-2)	2 (0-6)	10 (3-13)
Total Ankles (R&L)	11 (0-19)	3 (0-8)	12 (6-12)	18 (10-23)
Global Gait Scores	2 (0-4)	0 (0-1)	3 (1-4)	4 (3-4)
		HAL Domains: Median (range)		
TOTAL HAL	**80** (13.3-100) (54.2-94.6)	**90.4** (46-100) (IQR 76.7-98.1)	**71.7** (13-100) (IQR 57-87.1)	**49.5** (13.3-95.2) (IQR 40.5-69.5)
LSKS	**75** (10-100) (IQR 52.5-92.5)	**88.8** (47.5-100) (IQR 75-100)	**70** (7.5-100) (IQR 52.5-85)	**37.5** (10-100) (IQR 30-67.5)
LEGS	**66.7** (8.9-100) (IQR 40-91.1)	**82.2** (28.9-100) (IQR 66.7-97.8)	**55.6** (0-100) (IQR 40-80)	**28.9** (8.9-91.1) (IQR 22.2-60)
ARMS	**85** (10-100) (IQR 55.5-100)	**100** (25-100) (IQR 85-100)	**80** (10-100) (IQR 55-100)	**65** (10-90) (IQR 45-80)
TRANS	**86.7** (10-100) (IQR 60-100)	**96.7** (20-96.7) (IQR 80-100)	**80** (13-100) (IQR 60-100)	**50** (10-100) (IQR 33.3-100)
SELFC	**96** (20-100) (IQR 72-100)	**100** (20-100) (IQR 92-100)	**92** (20-100) (IQR 68-100)	**72** (20-100) (IQR 64-100)
HOUSEH	**93.3** (13.3-100) (IQR 63.3-100)	**100** (46.7-100) (IQR 90-100)	**86.7** (10-100) (IQR 63.3-100)	**70** (13.3-100) (IQR 53.3-93.3)
LEISPO	**80** (2.9-100) (IQR 56-96)	**91.4** (40-100) (IQR 71.4-100)	**73.3** (10-100) (IQR 56.7-88.6)	**52** (2.9-100) (IQR 40-80)
UPPER	**88.9** (17.8-100) (IQR 66.7-100)	**97.8** (42.2-100) (IQR 88.9-100)	**84.4** (10-100) (IQR 62.7-95.6)	**68.9** (17.8-95.6) (IQR 55.6-88.9)
LOWBAS	**70** (6.7-100) (IQR 50-96.7)	**86.7** (30-100) (IQR 66.7-100)	**63.3** (6.7-100) (IQR 53.3-90)	**36.7** (6.7-100) (IQR 26.7-63.3)
LOWCOM	**62.2** (0-100) (IQR 37.5-86.7)	**80** (37.5-100) (IQR 60-97.8)	**55** (4.4-100) (IQR 40-80)	**20** (0-91.1) (IQR 15.6-48.9)

(IQR =25th and 75th centile)

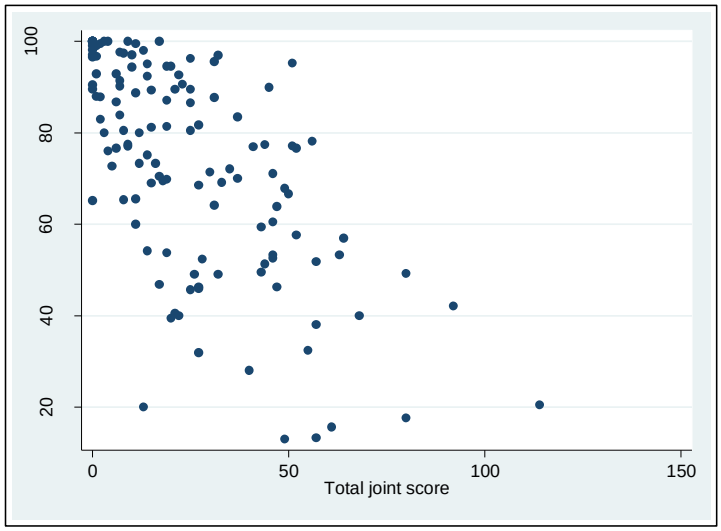
Table 4 – Correlation values between HAL domain scores and HJHS domain scores

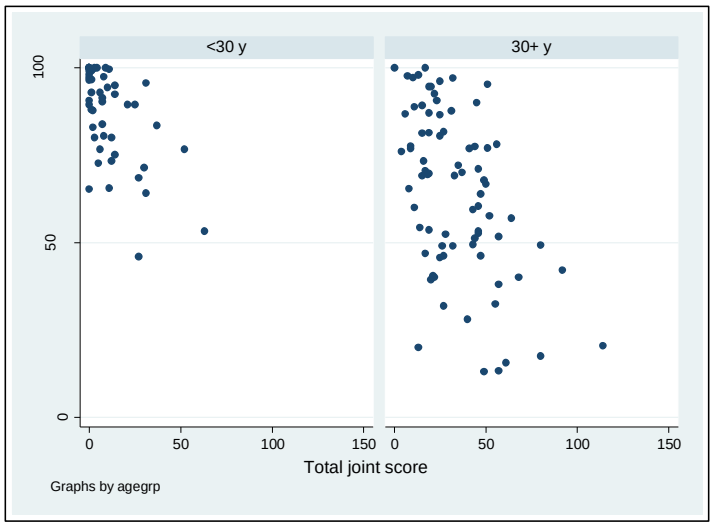
	HJHS											
	WHOLE GROUP (N=120)			Age: 18-30 (N= 50)			Age: 31-50 (N=47)			Age: 51-73 (N=23)		
	TOTAL SCORE	TOTAL LL	TOTAL UL	TOTAL SCORE	TOTAL LL	TOTAL UL	TOTAL SCORE	TOTAL LL	TOTAL UL	TOTAL SCORE	TOTAL LL	TOTAL UL
TOTAL SCORE	-0.66 *			-0.59 *			-0.41 *			-0.41 **		
LSKS		-0.64 *			-0.58 *			-0.25 **			-0.57 *	
LEGS		-0.60 *			-0.61 *			-0.37 **			-0.4	
ARMS			-0.60 *			-0.32			-0.46 *			-0.44 **
TRANS	-0.55 *			-0.43 *			-0.36 *			-0.53 **		
SELFC		-0.56 *	-0.56 *		-0.31	-0.02		-0.25 **	-0.45 *		-0.55 *	-0.36 **
HOUSEH	-0.47 **			-0.43 *			-0.25			-0.26		
LEISPO	-0.55 *			-0.5 *			-0.41 *			-0.22		
UPPER			-0.53 *			-0.38			-0.39 *			-0.43 **
LOWBAS		-0.58 *			-0.52 *			-0.32 **			-0.45	
LOWCOM		-0.66 *			-0.63 *			-0.4 *			-0.62 **	

*** Key:** ***=p<0.01** ****=p<0.05**

HJHS = Haemophilia Joint Health Score
HAL = Haemophilia Activities List
Total UL (upper limb) = right and left elbow scores
Total LL (lower limb) = right and left knee and ankle scores
LSKS: Lying down/sitting/kneeling/standing
LEGS: function of legs
ARMS: function of arms
TRANSP: Use of Transportation
SELFC: Self-care
HOUSEH: Household tasks
LEISPO: Leisure activities and sports
UPPER: Upper extremity activities
LOWBAS: Basic lower limb activities
LOWCOM: Complex lower extremity activities

Figure 1: Scattergraph to show relationship between total HAL and total joint score (a) in all patients (b) grouped according to age (<30 years and 30+ years) (HAL and HJHS)





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